

Application Serial No. 10/655,762

Office Action Mailed July 20, 2006

Amendment under 37 C.F.R. 1.116, Dated November 20, 2006

Listing of Claims

This listing of claims will replace all prior versions and listings of claims in the application.

1. (CURRENTLY AMENDED) A method for measuring the amount of at least two a target nucleic acid sequences in a biological sample, comprising the steps of:

- a) preparing a sample by ~~combining~~ adding in a sample the biological sample comprising the at least two target nucleic acid sequences and a known amount of at least two a standard nucleic acids, wherein said at least two standard nucleic acids has have a nucleotide sequence that is one base different than the respective target nucleic acid sequence ~~to a biological specimen containing the target nucleic acid~~;
- b) amplifying the sample of step a);
- c) using a further method to enhance ~~the~~ a mass difference between the at least two standard nucleic acid sequences and the at least two target nucleic acid sequences at the site wherein each of the standard nucleic acid sequence differs from the respective target nucleic acid sequence resulting in enhanced products with different masses so that the mass differences ~~created by the at least one base between the at least two standard and the at least two target nucleic acid sequences~~ can be detected; and
- d) quantifying the enhanced products of step c) by measuring the ratio of each of the amplified target nucleic acid to its corresponding ~~the~~ amplified standard nucleic acid to measure the amount of the at least two target nucleic acid sequences present in the biological sample, wherein the quantifying is performed using mass spectrometry.

2. (ORIGINAL) The method of claim 1, wherein ~~the~~ at least two target nucleic acid sequences are ~~is~~ from an infectious agent.

3. (ORIGINAL) The method of claim 1, wherein ~~the~~ at least two target nucleic acid sequences are ~~is an~~ mRNA transcripts.

4. (CANCELLED)

5. (ORIGINAL) The method of claim 1, wherein step c) is performed using primer extension at the site of differentiation.

Application Serial No. 10/655,762

Office Action Mailed July 20, 2006

Amendment under 37 C.F.R. 1.116, Dated November 20, 2006

6. (PREVIOUSLY PRESENTED) The method of claim 1, wherein step c) is performed using an enzyme that specifically cleaves at the site of differentiation.
7. (ORIGINAL) The method of claim 1, wherein step c) is performed using allele-specific hybridization at the site of differentiation.
8. (CURRENTLY AMENDED) The method of claim 1, 5, 6, or 7, wherein the quantifying is performed using MALDI-TOF mass spectrometry.
9. (CANCELLED)
10. (NEW) The method of claim 1, wherein one measures the amount of at least 5 target nucleic acid sequences using at least 5 respective standard nucleic acids.
11. (NEW) The method of claim 1, wherein one measures the amount of at least 10 target nucleic acid sequences using at least 10 respective standard nucleic acids.
12. (NEW) The method of claim 1, wherein one measures the amount of 25 target nucleic acid sequences using at least 25 respective standard nucleic acids.
13. (NEW) The method of claim 1, wherein one measures the amount of 50 target nucleic acid sequences using at least 50 respective standard nucleic acids.
14. (NEW) A method for measuring gene expression by measuring the amount of at least two target transcript sequences in a biological sample, comprising the steps of:
 - a) preparing a sample by combining in a sample the biological sample comprising the at least two target transcript sequences and a known amount of at least two standard nucleic acids, wherein said at least two standard nucleic acids have a nucleotide sequence that is one base different than the respective target transcript sequence;
 - b) amplifying the sample of step a);
 - c) using a further method to enhance the mass difference between the at least two standard nucleic acid sequences and the at least two target transcript sequences at a site of the one base difference wherein the standard differs from the target resulting in enhanced products with different masses so that the mass differences between the at least two standard and the at least two target transcript sequences can be detected; and
 - d) quantifying the enhanced products of step c) by measuring the ratio of each of the amplified target transcript to its corresponding amplified standard nucleic acid to measure the

Application Serial No. 10/655,762

Office Action Mailed July 20, 2006

Amendment under 37 C.F.R. 1.116, Dated November 20, 2006

amount of the at least two target transcript sequences present in the biological sample, wherein
the quantifying is performed using mass spectrometry.